form of definite symptoms from the bad mechanical use of the back are usually slow in coming. It is possible, however, to correct bad mechanical use of the back, and it is possible to fix rather firmly good habits even in the most unpromising individuals.

We are not prepared at this time to support the theory that many ailments of the nervous system or of the gastro-intestinal system are related to bad mechanical use of the body. We can, however, state that there is a frequent association of such symptoms with the mechanical use of the body. Our investigations have shown that albuminuria of young men which is not a true nephritis is associated almost exclusively with very bad mechanical use of the body. We believe that a sufficient case can be made out for correction as against compensation on the basis of actual ailments of the back and feet, generally conceded to be due to faulty use of the body even without the addition of possible symptoms connected with other organs.

We believe that physical training can only accomplish what it is expected to accomplish when it is based upon satisfactory fundamental principles and when bodily mechanics is regarded in a similar fashion as the disturbances of any other system of the body are regarded.

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# A CLINICAL STUDY OF WASSERMANN-FAST SYPHILIS, WITH SPECIAL REFERENCE TO PROGNOSIS AND TREATMENT.[1]

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The so-called Wassermann-fast syphilitic infection will probably attract increasing attention as the time during which modern methods of treatment have been employed lengthens and methods of intensifying the sensitiveness of the test demonstrate a smaller and smaller proportion of permanent negatives. A recent survey of the literature following a study of a group of apparently Wassermann-fast cases under treatment in the Section of Dermatology seems to suggest that while Wassermann-fastness is a type of syphilologic tradition, relatively little attention has been paid to critical clinical study of these cases, with a view to ascertaining the types of syphilis that may be expected to give rise to resistant positive reactions in the blood and whether the superficially asymptomatic character of certain of such cases is borne out by complete investigation. Without any predispositions on the matter we undertook to analyze the clinical picture presented by 101 apparently resistant infections, observed among 458 patients who had received more than twelve intravenous injections of arsphenamin, with appropriate interim mercurialization. While we do not suggest that the amount of treatment these patients received is to be regarded as conclusive evidence that they are Wassermann-fast, our experience has tended to show that patients who do not undergo a reversal of the blood Wassermann with this amount of treatment are likely to present resistant characteristics and will probably not be made negative without the employment of an amount of treatment which raises the question of the possibility of therapeutic injury instead of benefit. Kaplan, particularly, has been outspoken in his injunctions against attempting to reverse Wassermann-fast cases. Craig, on the other hand, has very properly emphasized the searching clinical examination, which must be made before a persistently positive blood Wassermann can be regarded as a solitary and insignificant symptom. It is to be feared that the decline in confidence which seems to have affected the persistent negative Wassermann as evidence of cure may have undesirable by-effects in a tendency to underestimate the persistent positive Wassermann as evidence of the clinical activity of the disease.

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[1] Presented before the Central Interurban Clinical Club, Rochester, May, 1920.

The 101 cases employed in this study were obtained from our records without predisposition with regard to the findings and have served as a valuable index of the lacks in completeness in our syphilologic examination. Particularly do we believe that closer attention to the condition of the cardiovascular system in patients with signs of resistant syphilitic infection will show that this group of structures may be the seat of pathologic change when the grosser visible manifestations such as cutaneous, osseous, and neurologic involvements have been brought under therapeutic control.

It is of interest to note that of the 101 cases in which serum Wassermann reactions resisted the amount of treatment described, only four (3.9 per cent.) were florid secondary cases at the time treatment was begun. The remaining 96.1 per cent. included, therefore, Wassermann positive latent cases and various forms of osseous, visceral, cutaneous, and neurologic syphilis and lues hereditaria. Data on the duration of the infection up to the time treatment on this service was begun were obtainable in only 35 per cent. of the cases, the period ranging from two months to twenty-four years, with an average duration of thirteen years. The duration of the presenting symptom averaged two and a half years (in 101 cases). The group, as a whole, therefore, is to be regarded as made up primarily of late syphilis.

**Methods of Examination.** The methods of examination employed in this group of cases included various combinations of twenty-one different groups of procedures (Table I). Since the work was undertaken without premeditation very few of the patients had routine or complete examinations as judged from such a schedule. On the other hand the majority of the examinations were more complete than in the average studies of syphilitic infections. The tabulations include the number of cases in which data were available in each type of special examination employed. It should be stated that the Wassermann test employed was performed under the direction of Sanford and consisted of a single Noguchi antigen test, using a rabbit-human hemolytic system with active serum and incubator fixation. Experience has shown this technic to be conservative so that fixed positives obtained with it would, with little doubt, prove persistently positive with any technic employing more highly fortified and multiple antigens or cold fixation.

TABLE I.—THE MULTIPLE PROCEDURE DIAGNOSTIC ATTACK ON SYPHILIS.

1. Intensive study of anamnesis.
2. The social estimation of the case.
3. The study of the family both in history and examination.
4. The serum Wassermann reaction (single antigen).
5. Modifications and intensifications of the serum Wassermann test, such as the provocative, cold fixation, multiple antigens, and Wassermann series.
6. The examination of the cerebrospinal fluid (two Wassermann tests, Nonne, cell count on the fresh fluid, colloidal gold test).
7. The dark-field examination and stains of fresh secretions.
8. The luetin test.
9. The Levaditi and other tissue stains.
10. The neurologic examination.
11. The eye examination.
12. The ear examination.
13. The nose and throat examination.
14. The dermatologic examination of the skin and mucous membranes.
15. Visceropathic studies of the liver and spleen and of the stomach, involving the study of anemias, blood dyscrasias, test-meals, esophagoscopy, roentgen examination, and so forth.
16. The special cardiovascular examination, including the physical findings, blood-pressure, electrocardiographic examination.
17. The roentgenologic examination.
18. Exploratory operative procedures (seldom used until after the therapeutic test).
19. Genito-urinary examination.
20. The therapeutic test.
21. Necropsy.

Table II indicates the number of patients in the Wassermann-fast group who were specially examined for the types of systemic involvement mentioned with the percentage showing syphilitic involvement before treatment was begun.

It will be apparent at once from Table II that cardiovascular syphilis among the patients specially examined for this form of involvement is the principal type of syphilis associated with a resistant positive Wassermann. This finding is in accord with the observations of Brown on the importance of a search for signs of aortitis in patients who are apparently Wassermann-fast. Of the group of thirty-five patients who had cardiovascular examinations 66 per cent. showed signs of early aortitis and 60 per cent. myocardial changes. There were no patients with hypertension (systolic blood-pressure over 140). It has seemed to us that the more we make systematic cardiovascular examinations of Wassermann-fast patients the more pathology we find. It is, of course, conceivable that a close inquiry into certain symptoms is directing our attention toward this group and allowing to pass unnoticed an equal grade of involvement in some more silent organ, such as the liver or spleen. Syphilis of the central nervous system and syphilis of the osseous system take second place in our experience, in spite of the belief voiced by Kaplan, for example, that a neurologic and cerebrospinal fluid examination in serum Wassermann-fast cases is likely to disclose evidence of general paresis. In 67 of the group of 70 patients who presented evidence of neurosyphilis, examination of both the cerebrospinal fluid and the nervous system was carried out and one or the other examination was done in the remaining 3. Of the twenty-one patients with neurosyphilis underlying their resistance to treatment 40 per cent. have proved to have paresis, 50 per cent. tabes, and 10 per cent. early cerebrospinal syphilis. It is, of course, conceivable that an unascertained proportion of the patients with resistant neurosyphilis of other clinical types than paresis will ultimately develop paresis. Attention will be called to the fact that cardiovascular and neurosyphilis are by no means mutually exclusive, since half the patients with neurosyphilis also had cardiovascular lesions.

TABLE II.—100 WASSERMANN-FAST(?) CASES; TABLE OF STRUCTURES PRESENTING EVIDENCE OF SYPHILITIC INVOLVEMENT BEFORE TREATMENT WAS BEGUN.

| System involved. | Number of cases examined. | Percentage showing syphilitic involvement. |
|---|---|---|
| Cardiovascular | 35[1] | 44 |
| Central nervous system | 70[2] | 30 |
| Osseous | 100[3] | 30 |
| Visceral (hepatic, splenic and gastric) | 100 | 21 |
| Cutaneous and mucous membrane | 100 | 17 |
| Lues hereditaria | 100 | 10 |
| Lues latens (positive Wassermann only) | 100 | 10 |

[1] Only the cases receiving special examination by Willius are considered.

[2] Only patients receiving special examination by Sheldon or spinal puncture, or both are considered.

[3] Does not include any routine roentgenologic examination.

The patients presenting osseous involvement failed to show any distinctive type of bone changes standing out preëminent in the group. Visceral involvement was represented by twenty-one patients, 52 per cent. of whom had gastric syphilis, 47 per cent. hepatic syphilis, and 14 per cent. splenic involvement. The large margin of error introduced into the proportions of hepatic and splenic syphilis by the impossibility of detecting by physical examination lesser degrees of involvement than those necessary to produce palpable tumor or recognizable symptoms must be borne in mind.

Cutaneous symptoms appeared in only 17 per cent. of the cases in our series, and in none of these was the cutaneous condition the sole manifestation of syphilis apart from the positive Wassermann. Nodular and infiltrative lesions served, on several occasions, as valuable clues to the infection, which in the absence of a gross indication for a Wassermann might have passed unrecognized. A particularly large percentage (50) in this group proved, on special cardiovascular examination, to present positive signs, a point which emphasizes the danger of skin-deep interpretation of syphilis and the imperative need to look back of the seemingly easily identified manifestations when a symptom such as Wassermann fastness appears. Only a small proportion (6 per cent.) of the resistant cases with cutaneous involvement presented evidence of neurosyphilis.

Heredosyphilis and syphilis whose existence is evidenced solely by a positive serum Wassermann reaction occupy only a small place among our resistant infections (10 per cent. each).

It is apparent, therefore, that Wassermann-resistant syphilis, far from being trivial or therapeutically minimizable syphilis, is synonymous with grave syphilis, involvement of the cardiovascular system, the nervous and the osseous structures, and the large viscera, constituting 70 per cent. of the total involvement.

Wassermann-resistant late syphilis, in addition to being grave syphilis, is polysymptomatic or exhibits a tendency to multiple structural involvement. This point is best brought out in Table III, in which each type of involvement is cross-indexed, so to speak, to the percentage of other forms of structural involvement associated with the presenting type. For example a patient whose presenting symptom was gummatous osteitis might be found on intensive study to have likewise a neurosyphilis and cardiovascular evidences of his infection. Complications of this sort whose clinical recognition should be the result of multiple diagnostic attack (Table I) have in the past been more conspicuous in the postmortem room than at the bedside, to the discomfiture of the clinician. Failure to recognize such complications during life should become increasingly rare as our clinical diagnostic armamentarium is improved and utilized.

We believe that it is worth while at this point to comment on the gradual approximation of clinical findings to necropsy findings which can be brought about by the use of group diagnosis in syphilis. To our minds there can be no more convincing evidence that syphilologic diagnosis will never resolve itself into the performance of any single technical test. We believe the logical method for identifying clinical syphilis in obscure cases is identical with that employed in the determination of the types of involvement in our Wassermann-fast cases, and consists essentially of a series of examinations by specialists, each expert in some particular phase of the disease. The results of such composite examination, and particularly the apparent demonstration that Wassermann-fast syphilis is a grave rather than a harmless affair, should compel the greatest conservatism in *ex cathedra* statements regarding the significance of seemingly monosymptomatic positive Wassermanns. Those who are inclined to interpret Wassermann positiveness as a favorable evidence of a high resistance to the infection, and hence of a probable freedom from complications, must, it seems to us, at least subject their material to the most searching and critical examination for every type of involvement before their conclusions can deserve general acceptance. That rash statements with regard to the insignificance of a fixed positive Wassermann may do harm and are to be discouraged until further evidence of its real meaning is available seems to us equally apparent.

TABLE III.—MULTIPLE STRUCTURAL INVOLVEMENT PRESENT IN EACH OF SIX TYPES OF SYPHILIS.

Of 15 patients with cardiovascular syphilis.
    20 per cent. also had neurosyphilis.
    20 per cent. also had osseous syphilis.
    20 per cent. also had cutaneous and mucous membrane syphilis.
    6 per cent. also had heredosyphilis.
    6 per cent. also had splenic, hepatic or gastric syphilis.
Of 21 patients with neurosyphilis.
    50 per cent. also had cardiovascular syphilis (of 6 specially examined).
    18 per cent. also had osseous syphilis.
    14 per cent. also had splenic, hepatic or gastric syphilis.
    4.6 per cent. also had cutaneous syphilis.
Of 30 patients with osseous syphilis.
    43 per cent. also had cardiovascular syphilis (of 6 specially examined).
    17 per cent. also had cutaneous syphilis.
    13 per cent. also had neurosyphilis.
    10 per cent. also had visceral syphilis.
Of 21 patients with visceral syphilis (splenic, hepatic or gastric).
    14 per cent. also had cardiovascular syphilis (of 7 specially examined).
    25 per cent. also had neurosyphilis.
    14 per cent. also had osseous syphilis.
Of 17 patients with cutaneous and mucous membrane syphilis.
    50 per cent. also had cardiovascular syphilis (of 6 specially examined).
    6 per cent. also had neurosyphilis.
    30 per cent. also had osseous syphilis.
Of 10 patients with heredosyphilis.
    33 per cent. also had cardiovascular syphilis (only 3 specially examined).
    20 per cent. also had neurosyphilis.
    20 per cent. also had osseous syphilis.
    40 per cent. also had interstitial keratitis.
    30 per cent. also had eighth nerve deafness.

Three points stand out conspicuously from the foregoing study: (1) The more carefully the search for cardiovascular syphilis is carried out in Wassermann-fast cases which exhibit other signs of active disease on first examination the more often cardiovascular syphilis is recognized. This finding is in accord with necropsy experience with syphilis in general, as presented by Warthin, Symmers and others. The former in particular found the heart and aorta involved to some degree in every case and rates myocarditis as the most common cause of death from syphilis. (2) Wassermann-resistant patients who have some definite clinical manifestation of syphilis as a presenting symptom on superficial examination are likely to exhibit multiple types of involvement on complete examination. The type of infection presenting a resistant positive Wassermann is therefore probably not produced by a special strain of organism, and Wassermann fastness should therefore probably be interpreted less as a single symptom than as a guide to an underlying multiplicity of symptoms. The conspicuous exception is the long-recognized inverse relationship between cutaneous and neurosyphilis which seems to be the only example of a mutually exclusive combination in the series. (3) The last point suggested by this study is that there is a curious, almost paradoxical contrast between syphilis whose only symptom after careful examination is a positive Wassermann and syphilis with both active lesions and a positive Wassermann whose resistant character becomes apparent only after treatment. Our group of such pure latent cases is too small and our period of observation too short to justify a prediction as to whether these patients will ever develop active manifestations. We do not therefore offer here any generalizations on the possible protective significance of the monosymptomatic serum Wassermann. That only 10 per cent. of such monosymptomatic Wassermanns appeared in our series suggests at least that the group in which Wassermann-fastness can be dismissed as meaningless is very small.

Certain incidental observations from our series are based on groups of cases too small as yet to deserve detailed analysis. One such interesting incidental finding was the presence of septic foci in teeth, tonsils, and elsewhere in 74 per cent. of the cases. We are not prepared to suggest the relation of this detail to the resistant Wassermann or to the polysymptomatic character of the infections in this group. In 29 per cent. of the cases the foci were removed without effect on the Wassermann. Only 12 per cent. of the patients were users of alcohol. In view of the well-known inhibitory effect of acute alcoholism on the positive serum-Wassermann reaction such a finding may ultimately prove of interest. There was no evidence that pregnancy and childbearing had any relation to the resistant Wassermann reaction.

**Treatment of the Resistant Wassermann Patients.** It will be recalled that for the purposes of this paper we defined our Wassermann resistant group as consisting of those cases which were not permanently reversed to negative in the blood by a minimum of twelve injections of arsphenamin and interim mercurialization by inunction. This amount of treatment left Wassermann positive only four of the early cases seen on the service. It appears, therefore, that the resistant Wassermann in our experience is a manifestation of late syphilis (average duration of disease thirteen years in 35 cases and of symptoms two and a half years in 90 cases). An analytical *resume* of our treatment technic in these cases is as follows:

| | |
|---|---|
| Minimum number of arsphenamin injections | 12 |
| Maximum number of arsphenamin injections | 29 |
| Average number of injections for each patient | 14 |
| Average number of injections for each course | 6 |
| Average number of courses for each patient | 2⅓ |
| Average period over which the above treatment was given | 11 months |
| Average interval between injections | 1 week |
| Average total duration of arsphenamin treatment | 2½ months |
| Average number of inunctions given (90 patients) | 90, 4 gm. 33 per cent. |
| Average number of inunctions given for each course | 40 |
| Average number of succinimid injections given (21 patients) | 21, ⅙ gr. daily |
| Average total duration of inunction treatment | 4¼ months |

Summarizing, it appears that the average Wassermann resistant patient in our series remained Wassermann positive after fourteen arsphenamin injections and ninety 4 gm. 33 per cent. inunctions administered intermittently in eleven months and equivalent to about six months' continuous treatment. It should be mentioned that we often employ arsphenamin and mercury simultaneously, thus shortening the continuous period as compared with the intermittent period.

This amount of treatment, then, has secured the reversal of about 96 per cent. of our early cases and 78 per cent. of our late cases. It is interesting, for example, that Detweiler reports 57 per cent. of a large series reversed by eight injections of diarsenol. The fallacy of comparisons between such series is easily appreciated by recalling that the serum-Wassermann reaction has no standard meaning for all observers. An insensitive test which is a valuable guide to Wassermann fastness is a poor guide to therapeutic effect, since in the former it picks out as fixed positives cases whose Wassermann reactions would certainly be positive with hypersensitive antigens or cold fixation, while in the latter it results in premature negatives which a sensitive technic would still recognize as positives. An observer using a hypersensitive Wassermann therefore secures fewer reversals than one using a conservative technic. We find ourselves in full accord with Wile and Hasley in refusing to accept even a persistent negative Wassermann reaction as evidence of cure, since its meaning is largely a matter of technic. The present study, however, compels us to reserve our opinion on their espousal of the obverse view that "in the presence of an intensive therapy a positive test does not mean living spirochetes and a potential syphilis."

So far as symptomatic therapeutic effects are concerned the clinical results in our series of 101 Wassermann-resistant cases were much more satisfactory than the serologic. In 84 per cent., in spite of the persistent positive Wassermann, the infection was symptomatically arrested *pro tempore* and the visible lesions disappeared. In 16 per cent. the disease continued to progress or clinical evidence of active syphilis persisted. Of the 16 patients not responding to the above therapy, 6 had paresis, 3 had gastric crises in tabes dorsalis, 2 had cerebrospinal syphilis, 2 had interstitial hepatitis, 1 cyclic vomiting, 1 myocardial degeneration, and 1 a persistent anemia. We wish to enjoin conservatism in the attempt to make ultimate interpretations of the above results. Regardless of the degree of symptomatic improvement achieved no one of our series of patients will be voluntarily dismissed by us from observation throughout life.

The question of the amount of treatment which it is proper to administer to a Wassermann-resistant patient is no more susceptible of exact definition and reply than are the many other questions centering around the problem of standard procedures in syphilotherapy. With the immunologic meaning of the complement-deviation test still obscure, the first essential to a decision is lacking. The second essential, too generally overlooked, is almost as far from adequate understanding. Until we have a more exact comprehension of the harm which excessive treatment may inflict on the body, and notably on the excretory mechanism and on tissues on which the treatment employed has a selective toxic effect, we cannot, at least in late and Wassermann-fast cases, make that exact estimation of balance between the potential evils of the disease and the evils of therapy which the occasion demands. We have therefore adopted as guides to treatment tentative principles as follows:

1. Search every accessible organ and tissue in the Wassermann-fast case by every clinically available method for evidence of syphilitic changes.
2. Weigh the degree of activity of the process and the extent of damage and probable recuperative power of the most vital structure involved by the infection.
3. Identify the weakest element in the patient's make up and estimate the tolerance for arsenic and mercury of the structures which must bear the brunt of treatment by-effects, such as the liver, kidney, and skin.

4. Do all that can be done to increase tolerance of treatment by protective measures, by extirpation of focal infection and by selection of the therapeutic agents.

5. Direct the treatment of Wassermann-resistant patients less toward overcoming the resistance offered by the Wassermann reaction and more toward a satisfactory symptomatic response of the vital structures involved by the disease within the limitations imposed by the weakest element in the tolerance. Get all the symptomatic effect possible short of recognizable damage. If tolerance permits give at least as much treatment as to a fully developed secondary case.

6. Recall the fallibility of human judgment, which in syphilotherapy at least has had neither the time nor the means to achieve conclusive results, and always regard the Wassermann-fast patient as potentially syphilitic, and for that reason not to be dismissed from careful search for evidence of activity at intervals throughout life.

**Summary.** 1. Of 458 syphilitic patients who had received from twelve to twenty-nine arsphenamin injections combined with mercurial inunctions, the average being fourteen injections and ninety inunctions in eleven months, 6.6 per cent. of primary and secondary cases and 101, 22 per cent., of latent, late and hereditary cases (average duration thirteen years) remained persistently Wassermann positive.

2. Cardiovascular changes are apparently those most likely to underlie a resistant positive Wassermann test in late syphilis (44 per cent.), with neurosyphilis 30 per cent., osseous lesions 30 per cent., hepatic, splenic, and gastric syphilis 21 per cent., and other types from 10 to 17 per cent.

3. More than one type of involvement was the rule in the individual cases of this group. There were only 10 patients presenting no other evidence of syphilis than their positive Wassermanns.

4. Patients with syphilis should therefore be studied from other angles than that of the presenting type of involvement, in the effort properly to appraise their condition and susceptibility to treatment.

5. Sixty-five per cent. of the patients with cardiovascular syphilis had aortitis and 60 per cent. myocardial changes.

6. Of the neurosyphilitics, 40 per cent. had paresis and 50 per cent. clinical tabes dorsalis.

7. Fifty per cent. of patients with neurosyphilis had cardiovascular syphilis also.

8. Gastric and hepatic syphilis were recognized in 52 and 47 per cent. of the visceral cases as against only 14 per cent. presenting recognizable splenic involvement. Patients with cutaneous syphilis showed the familiar immunity from neurosyphilis and the reverse.

9. While pyogenic foci were present in 74 per cent. of the patients with resistant-Wassermann reactions no frank etiologic connection

was apparent. The same was true of alcohol, which was used by only 12 per cent. of these patients.

10. There was no evidence that Wassermann-fastness is the result of infection with any special strain of organism. In fact, the "polystructural" involvement in such cases suggests the contrary.

11. Eighty-four per cent. of the patients in our Wassermann-resistant group have undergone symptomatic arrest today under the treatment received. Paresis and tabes dorsalis with gastric crises formed more than half the failures.

12. The amount of treatment to which a Wassermann-resistant patient should be subjected cannot be exactly defined. The principles employed in making a decision, which are in effect the principles underlying the therapy of all late syphilis, are outlined on page 666. In particular, reversal of the Wassermann, while desirable, should not be the primary aim of the therapy. Symptomatic response, with arrest of the process, and the giving of as much treatment as to an early case, provided tolerance permits, are the important considerations.

13. A persistently positive serum Wassermann reaction seems to be an accompaniment of grave rather than of trivial syphilis. At least such is the case in enough instances to suggest the need for the most painstaking and repeated investigation of the clinical aspects of the Wassermann-fast case. Premature statements based on insufficient evidence as to the insignificance of a fixed positive Wassermann reaction are, we believe, to be deprecated.

14. Wassermann-fast patients should not, in our opinion, be discharged from periodic careful reëxamination, with special reference to the cardiovascular and nervous systems throughout life. The frequency of such examinations should be dictated by the gravity and extent of the original process and the degree of apparent resistance to treatment.

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